International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Serum Leptin and Lipid Profile in Lichen Planus: A Case Control Study

Sarkar M[1], Dayal S[2], Samanta S[3], Ghalaut V.S[4], Malik I[5], Sehgal P. K[6]

[1]Junior Resident, Department of Biochemistry. PT. B. D. SHARMA PGIMS Rohtak.
[2]Professor, Department of Dermatology &Venereology .PT. B. D. SHARMA PGIMS Rohtak.
[3]Senior Resident, Department of Critical Care Medicine. SGPGI Lucknow.
[4]Sr. Professor and Head, Department of Biochemistry.PT. B. D. SHARMA PGIMS Rohtak.
[5]Assistant Professor, Department of Biochemistry. PT. B. D. SHARMA PGIMS Rohtak.
[6]Professor and Head, Department of Blood Transfusion. PT. B. D. SHARMA PGIMS Rohtak.

Corresponding Author: Sarkar M.

Received: 15/09/2015 *Revised: 28/09/2015* *Accepted: 30/09/2015*

ABSTRACT

Objective: Lichen planus (LP) is a common chronic inflammatory disease involving the skin and mucous membranes. Its etiology is thought to be autoimmune as various cytokines are involved in LP similar to psoriasis, which is a disease having autoimmune origin. Leptin, an adipocyte-derived hormone, plays a role in immune responses and promotes autoimmunity. Dyslipidemia is associated with LP hence this study was conducted to determine serum leptin levels along with lipid profile in LP patients.
Material and Methods: This prospective case control study was conducted in Department of Biochemistry from February 2014 to March2015. Twenty five clinically diagnosed patients of LP attending the outpatient Department of Dermatology and Venereology were enrolled for the study after taking written consent. The serum leptin level was measured by ELISA technique and lipid profile by enzymatic method. The results were compared with twenty five age and sex matched healthy controls.
Results: Serum leptin and lipid profile levels in 25 patients of LP and 25 age-sex matched healthy volunteers were analysed in this study. Leptin level was found to be significantly higher in LP group as compared to healthy volunteers ($p < 0.05$). We also found positive correlation between duration of illness in LP and serum leptin level. Among lipid profile parameters TC, LDL and TG were significantly higher in LP group as compared to healthy control (p value<0.05). HDL and VLDL were comparable between LP and healthy control group.
Conclusion: Hyperleptinemia is associated with LP. It may have role in the pathogenesis or severity of lichen planus. We recommend monitoring of lipid profile and serum leptin levels in these patients to prevent long term cardiovascular sequel. However further large scale studies are required to prove the hypothesis.

Keywords: Leptin, Lipid profile, Lichen planus.

INTRODUCTION

Lichen Planus (LP) is a chronic inflammatory autoimmune mucocutaneous disease which can affect skin, mucous membrane, appendages, genital mucosa, nails and scalp. This disease is more common in middle aged patients & females are more involved than males. [1] Clinically it presents as white striation (wickhamstriae), white papules, erythema,

erosions or blisters. [2] Buccal mucosa, dorsum of tongue and gingiva are commonly affected.

Its etiology is autoimmune as various cytokines are involved in LP similar to psoriasis, which is a disease having autoimmune origin. Leptin, an adipocyte-derived hormone, plays a role in immune responses and promotes autoimmunity. Oral LP is associated with T-cell mediated autoimmune disease in which autocytotoxic CD8+ cells trigger the apoptosis of oral epithelial cell. [3,4]

Leptin is a polypeptide hormone secreted by white adipose tissue. [3,4] Several studies confirmed rise in leptin level in individuals with high BMI and percentage total body fat. [5,6] It also plays a role in cellular immune response and promotes autoimmunity. It has been proposed that leptin promotes synthesis of cytokines and modulates helper T cell, thus might be involved in the pathogenesis of psoriasis. [7-9] There is limited literature on leptin status in other dermatological disease except psoriasis. [10-13] It might have a potential role in pathogenesis in LP. However there is paucity of literature regarding the leptin levels in LP.

Dyslipidemia is also associated with LP. In many studies, it has been shown that lipid profile levels are significantly altered in LP as compared to normal healthy control group and they concluded that there is a relation between chronic inflammation and dyslipidemia that increases the risk of cardiovascular diseases. [14,15]

It is of interest, whether leptin can influence the development of LP. To the best of our knowledge there is no previous literature on serum leptin levels in patients with LP. The aim of this study was to compare serum leptin levels in recently diagnosed LP patients and healthy controls. We also evaluated the relation between leptin levels, lipid profile and duration of illness.

MATERIALS AND METHODS

The prospective case control study was conducted in the Department of Biochemistry in collaboration with Department of Dermatology in Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak. It was performed from February 2014 to March2015. Twenty five clinically diagnosed patients of LP attending the Outpatient Department of Dermatology and Venerology were enrolled for the study after taking written consent. The serum leptin level was measured by ELISA technique and lipid profile by enzymatic method. The results were compared with 25 age and sex matched healthy controls.

During the time period of study, subjects were recruited prospectively and consecutively after meeting inclusion criteria, which were new clinically diagnosed cases of LP not on any treatment for last four weeks. We selected age- and sex-matched healthy controls from healthy hospital staffs not affected by LP or other autoimmune diseases. Subjects in our study were aged from 20 to 60years.

Patients under treatment with systemic corticosteroids, lipid lowering agents, thiazides, retinoids, beta blockers, methotrexate, cyclosporine and immunosuppressive were excluded. All known cases of kidney disease, liver disease, ischemic heart disease, neurological disease, endocrine disorders, malignancy, pregnant or lactating women, patients undergone major surgery or trauma and having drug addiction were also excluded.

Complete history and physical examination with anthropometry were performed in controls and cases. Serum leptin and lipid profile were done before start of medication in the cases.

Data Collection: Detailed history regarding all demographic parameters (age, sex, BMI, socioeconomic status, addictions, duration of disease), any systemic illness or any drug intake was taken. Routine biochemical

parameters, lipid profile and serum leptin levels were measured and respective data was recorded.

Sample Collection and Storage: Six mL of fasting (12 hr fasting) venous blood sample was taken in a plain red capped evacuated blood collection tube under all aseptic precautions. Samples were processed within one hour of collection. Serum was separated by centrifugation at 2000 rpm for 10 minutes after clotting. Routine investigations were done on the same day and rest of the serum stored at -20^{0}C for serum leptin estimation for subsequent analysis.

All routine investigations including lipid profile were done in autoanalyzer using enzymatic method.

Serum Lipid Profile: TG was estimated in autoanalyzer (Randox) by enzymatic method. The TG level determined after enzymatic hydrolysis with lipases. The indicator, quinoneimine formed from hydrogen-peroxide, 4-aminophenazone and 4-chlorophenol under the catalytic influence of peroxidise. [16]

TC estimated by enzymatic method in autoanalyzer (Randox). The cholesterol is determined after enzymatic hydrolysis and oxidation. The indicator quinoneimine is formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidise. [16]

HDL estimated in autoanalyzer (Randox) by enzymatic method. The enzymes cholesterol esterase, cholesterol oxidase and peroxidase are used with 4-AA and HDAOS as indicator after chylomicron, VLDL-C and LDL-C is eliminated. [16]

LDL-C was determined by Friedewald equation. [11] VLDL-C was obtained by formula. [17]

Serum Leptin: DRG Leptin ELISA (enzyme immunoassay for quantitative in vitro diagnostic measurement of Leptin in serum and plasma) kit was used. [18]

Principle of the Test: DRG Leptin ELISA kit is a solid phase enzyme linked immunosorbent assay based on the sandwich principle. Microtiter wells were coated with a monoclonal antibody directed towards a unique antigenic site on leptin molecule. An aliquot of patient sample containing endogenous leptin was incubated in specific well with biotinylated monoclonal anti Leptin antibody. A sandwich complex was formed after incubation the unbound material was washed off and a Peroxidise enzyme complex was added for detection of the bound leptin. After adding the substrate solution the intensity of color developed is proportional to the concentration of leptin in the sample.

Statistical Analysis: Statistical analysis was carried out by standard statistical software SPSS version 18 using appropriate statistical tests. Data were expressed as mean± SD, median and confidence interval (CI), frequency or number as appropriate. Categorical variables were analysed with Pearson Chi Square Test. Comparison among two groups for different parameters like leptin and lipid profile was analysed using student t test or Mann Whitney U test. Pearson correlation was used to examine the strength of correlation among the parameters, serum leptin level and lipid profile. For all statistical tests P value <0.05 was considered as significant.

RESULTS

A total of 50 subjects were included in the study, first group comprising of 25 patients with LP and 25 healthy volunteers as control in second group. Age, gender and BMI distribution were comparable between two groups (Table1). Leptin levels were significantly higher in LP group compared to healthy volunteers (p value< 0.05, Table 2, Figure1). In mucocutaneous form of LP, leptin was found to be significantly higher compared to other forms, such as cutaneous and oral LP (OLP) (p value<0.05, Table 3,

Figure 2). Overall female had slightly higher leptin level compared to male which was expressed as mean±SD found to be 20.50±18.86, 15.26±13.82 respectively (p value >0.05). It was also statistically significant (p >0.05).In LP group leptin level was little higher in patients with high BMI (>25) compared to low BMI (≤25) group but statistically comparable (p value> 0.05, Table 4, Figure 3). Duration of illness in LP showed positive correlation with serum leptin levels (r value=0.651, p value < 0.05*, Figure 4).

Among lipid profile parameters TC, LDL and TG was significantly higher in LP group compared to healthy control (p value<0.05, Table5, Figure 5). HDL and VLDL were comparable between LP and healthy control group, but statistically not significant.

High (>25) and low (≤25) BMI subgroup in LP patients had statistically comparable lipid profile parameters (Table6, Figure 6). Overall male had higher HDL level compared to female expressed as mean ±SD and found to be 43.43 ± 2.65 vs 39.34 ± 4.61 (p value < 0.05*). Other lipid profile parameters had no gender variation.

Table 1: Demographic characteristics

Parameters	Lichen planus (n=25)	Healthy volunteers (n=25)	P value
Age in years (mean ± SD)	37.52±12.70	40.60±7.72	0.305
BMI (kg/m^2)(mean ± SD)	27.18±3.16	27.05±3.14	0.881
Gender(M/F)	8/17	13/12	0.152
Forms of illness	Cutaneous-15 Mucocutaneous-8 Oral-2	-	-

Table 2: Serum leptin level in two groups

Parameters	Lichen planus (n=25)	Healthy volunteers(n=25)	P value
Leptin (ng/ml) (Mean±SD)(CI)	25.83± 20.85 (18.28-35.08)	10.76 ± 5.93 (8.57-13.19)	0.001*

*Significant

Table 3: Leptin level in different forms of Lichen planus

Parameters	Mucocutaneous LP	Cutaneous LP	Oral LP	P value
Leptin(ng/ml) (Mean±SD)(CI)	40.71±16.91 (28.93-51.51)	20.35±19.87 (12.15-32.15)	7.39±2.61 (5.54-9.24)	0.028*

*Significant

Table 4: Leptin level and BMI in lichen planus patients

Parameter	BMI>25	BMI≤25	P value
Leptin(ng/ml) (Mean± SD)(CI)	27.61±22.57 (18.14-37.58)	18.71±10.51 (10.70-28.42)	0.405

Table 5: Lipid profile in two groups

Parameters	Lichen planus (n=25)	Healthy volunteers (n=25)	P value
TC (mg/dl)(mean ± SD)	215.36± 63.4	159.08 ±18.36	0.00*
TG (mg/dl)(mean ± SD)	185.32±82.69	132.32±37.52	0.00*
HDL (mg/dl)(mean ± SD)	41.08±4.35	41.04±4.49	0.97
LDL (mg/dl) (mean ± SD)	142.84 ± 62.33	84.56 ± 21.09	0.00*
VLDL (mg/dl)(mean ±SD)	34.84 ± 15.48	33.48±14.53	0.75

*Significant

Table 6: Lipid profile and BMI in lichen planus patients

Parameter	BMI(≤25)	BMI(>25)	P value
TC (mg/dl)(mean ± SD)	201.40 ± 74.84	218.85 ± 61.92	0.59
TG (mg/dl)(mean ± SD)	156.60±60.49	192.50±87.16	0.39
HDL (mg/dl)(mean ± SD)	40.80±4.91	41.15±4.34	0.87
LDL (mg/dl)(mean ± SD)	119.6 ±57.2	148.65 ± 63.57	0.36
VLDL (mg/dl)(mean ± SD)	33.80±14.56	35.10 ± 16.05	0.87

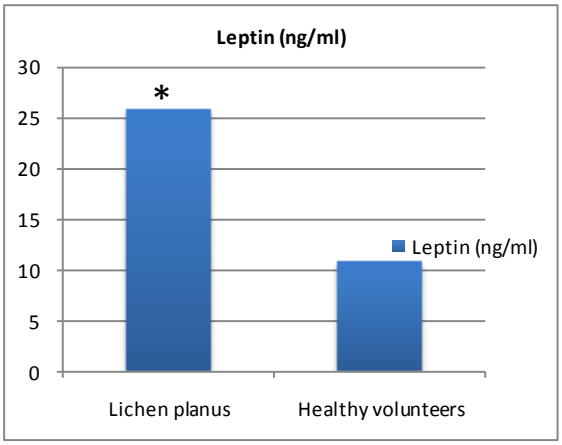

Figure 1: Serum Leptin level in two group
*** p value <0.05**

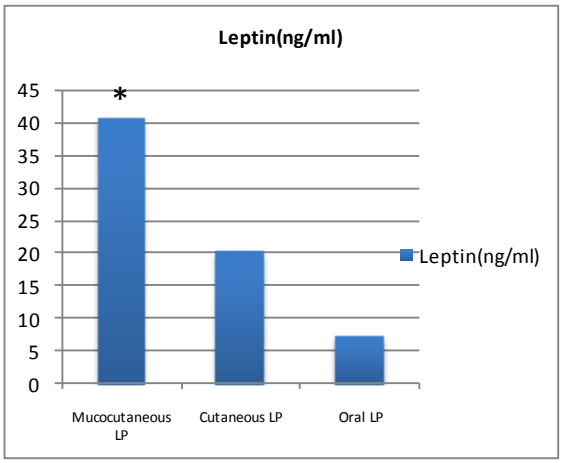

Figure 2: Leptin level in different forms of lichen planus
*** P value <0.05**

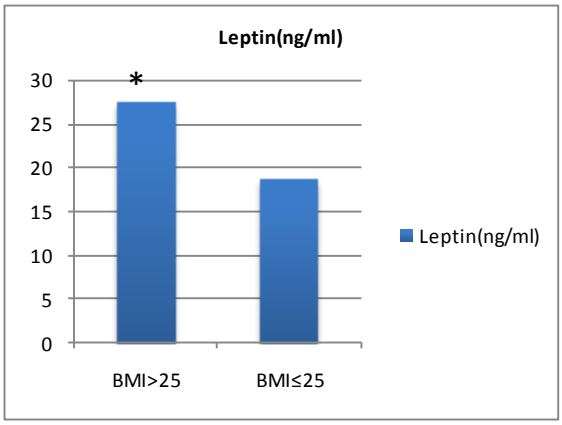

Figure 3: showing serum leptin level in high(BMI>25) and low BMI(≤25) subgroup
.* p value <0.05

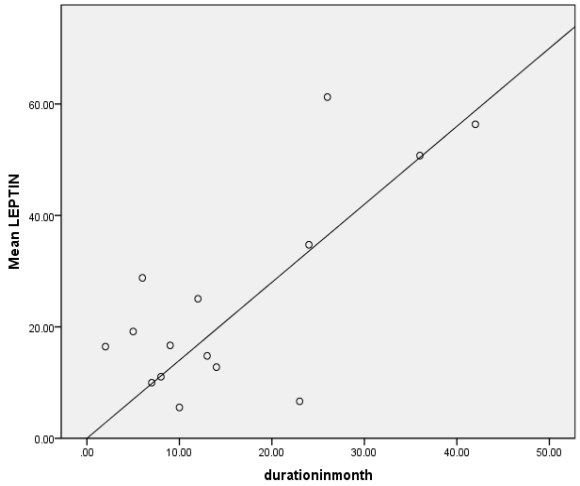

Figure 4: Scatter plot showing correlation between leptin and duration of illness of lichen planus

DISCUSSIONS

We conducted a prospective observational study in newly diagnosed LP patients. Our aim was to study serum leptin and lipid profile in LP patients and to compare it with healthy volunteers.

This has been well confirmed in studies showing rise in circulating leptin levels in relation to BMI and percentage total body fat. [8,9]

Hyperleptinemia is common in psoriatic patients. In a meta-analysis in 2013 Zhu K. J. et al identified total 11 studies, comprising 73 patients with psoriasis and 570 healthy controls and observed that serum leptin level was increased in patients with psoriasis compared with those in controls. [10] In psoriasis group leptin level was significantly higher in patients with higher PASI score (>15) compared to low PASI score (<15) in previous studies by Aktan et al, Cerman et al and Zayed et al. [11-13]

There is limited literature available on serum leptin status in other dermatological disease except in psoriasis. After detailed scanning of literature no studies were found related to leptin levels in LP. To the best of our knowledge our study is not preceded by any similar study. In our study we found significantly higher levels of

serum leptin in LP group as compared to healthy control group ($p < 0.05$). LP is a autoimmune disease involving activation of cluster differentiating factor-8 positive (CD-8 +)T- cells and also CD-4 + T- cells, release of different cytokines such as interleukine (IL) -12 , IL-2 and interferon-ɣ. We may associate the rise of leptin, which itself triggers immune response and promotes autoimmunity, in LP patients to pathogenesis of the disease.

In LP, mucocutaneous form of disease had significantly higher leptin level compared to other forms such as cutaneous and OLP (p value <.0.05). Since mucocutaneous LP is extensive form of disease the levels of inflammation, cytokine release and immunological process is much widely spread as compared to the localised oral and cutaneous form of disease. BMI had no significant effect on leptin level in LP patients (p value > 0.05). However we found a positive correlation between duration of illness in lichen planus and serum leptin level($r = 0.674$, p value < 0.05). This finding is itself self explanatory that it might have role in pathogenesis of the disease.

In literatures there are conflicting results on serum lipid values in chronic inflammatory skin disease. J. Dreiher et al conducted a case control study in Israel to evaluate the dyslipidemia in LPand found significantly high lipid profile parameters in patients with LP (42.5% vs 37.8%, p= 0.003, odds ratio, OR1.21, 95% confidence interval, [CI]:1.06-1.38). [14] Bhuvana K et al conducted a case control study on 32 adults of which 18 with either OLP or oral lichenoid reactions (OLR) and 14 age and sex matched healthy controls. They found increased levels of TC and LDL-C in OLP and OLR patients when compared to normal healthy individuals. They also found significantly higher TG and VLDL in OLP when compared to OLR and lower HDL-C levels in OLP when compared to OLR. They concluded that there may be an association between chronic inflammation and dyslipidemia that increases the risk for cardiovascular disease. OLP and OLR patients have increased serum cholesterol and LDL-C when compared to normal adults. [15]

In our study TC, LDL and TG were significantly higher in LP group compared to healthy control (p value<0.05). HDL and VLDL were comparable between LP and healthy control group and not statistically significant. Although in LP patients BMI had no significant impact on lipid profile. Our study is more or less in accordance with the previous studies on LP regarding the above parameters.

However we have several limitations in our study. We included small number of patients (25 in each group. Since cases were taken from outpatient department of dermatology we could not include various morphological form of LP in our study as found in general population and these may affect our results.

In conclusion, as higher leptin level is found in patient with LP it may have possible role in pathogenesis or severity of the disease. Patient with LP also have associated lipid profile abnormalities. We recommend monitoring of lipid profile and serum leptin levels in these patients to prevent long term cardiovascular sequel and for better prognosis. However further large scale studies are required to substantiate our findings and prove the hypothesis.

REFERENCES

1. Sugerman PB, Savage NW, Walsh LJ, Zhao ZZ, Zhou XJ, Khan A, et al. The pathogenesis of oral lichenplanus. Crit Rev Oral Biol Med 2002; 13:350-65.
2. Andreasn JO. A clinical evaluation of 115 cases. Oral Surg Oral Med Oral Pathol 1968; 25:31-42.
3. Kumari A, Suman B, Sharma, Singal A, Aggarwal A. Association of carotid intima-media thickness with leptin and apolipoprotein b/apolipoprotein a-i ratio

reveals imminent predictors of subclinical atherosclerosis in psoriasis patients. Actamedica 2014; 57:21–7.
4. Vanizor Kural B, Örem A, Çimşit GU, Yandi YE, Calapoglu M. Evaluation of the atherogenic tendency of lipids and lipoprotein content and their relationships with oxidant-antioxidant system in patients with psoriasis. Clinica Chimica Acta 2003; 328:71-82.
5. Hercogová J, Ricceri F, Tripo L, Lotti T, Prignano F. Psoriasis and body mass index. Dermatol Ther 2010; 23:152-4.
6. Kimball AB, Gladman D, Gelfand JM. National Psoriasis Foundation clinical consensus on psoriasis comorbidities and recommendations for screening. J Am Acad Dermatol 2008; 58(6):1031-42.
7. Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. Lancet 2007; 370(9583):263-71.
8. Maffei M, Halaas J, Ravussin E, Pratley R, Lee G, Zhang Y, et al. Leptin levels in human and rodent: measurement of plasma leptin and ob RNA in obese and weight-reduced subjects. Nat Med 1995;1(11):1155–61.
9. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. New Engl J Med 1996; 334(5):292–5.
10. Zhu KJ, Zhang C, Li M, Zhu CY, Shi G, Fan YM. Leptin levels in patients with psoriasis: a meta-analysis. Clin Exp Dermatol 2013;38:478-83
11. Cerman. AA; Bozkurt, S.; Sav, A. Serum leptin levels, skin leptin and leptin receptor expression in psoriasis. Br J Dermatol2008; 159:820-826
12. Aktan S, Rota S, Erdogan BS, Ergin S, Kaptanoglu B, Bostanci M. A Role OfLeptin in Psoriasis. Turk J Med Sci 2007; 37:135-8.
13. Zayed AA, Maksoud NA, Ragab HM. Psoriasis vulgaris severity and body mass index: evaluating the role of leptin, tumor necrosis factor-a, and interleukin-6. Journal of the Egyptian Women's DermatologicSociety 2012, 9:86-91.
14. J Dreiher, J Shapiro, A.D. Cohen. Lichen planus and dyslipidemia: A case control study. Br J Dermatology 2009; 161(3):626-9.
15. Bhuvana K, Suma GN, Mamatha N S, Sowbhagya M B, Komali G. Lipid Profile and Metabolic Syndrome Status in Patients with Oral Lichen Planus, Oral Lichenoid Reaction and Healthy Individuals Attending a Dental College in Northern India - A Descriptive Study. Journal of Clinical and Diagnostic Research 2014; 8: 92-5.
16. Warnick GR, Nauch M, Rifai N. Evolution of method for measurement of HDL-cholesterol: from ultracentrifugation to homogeneous assays. Clin Chem 2001; 47:1579-96.
17. Rifai N, Iannotti E, DeAngelis K, Law T. Analytical and clinical performance of a homogeneous enzymatic LDL-cholesterol assay compared with the ultracentrifugation-dextran sulphate-Mg++ method. Clin Chem 1998; 44:1242-50.
18. Imagawa K, Matsumoto Y, Numata Y, Morita A, Kikuoka S, Tamaki M et al. Development of a sensitive ELISA for human leptin, using monoclonal antibodies. Clin Chem 2001;47:1579-96.

How to cite this article: Sarkar M, Dayal S, Samanta S et al. Serum leptin and lipid profile in lichen planus: A case control study. Int J Health Sci Res. 2015; 5(10):129-135.

****